## REMARKS

Claims 66-79 are added. Therefore, claims 56-59 and 62-79 are pending. Claims 56 and 62 are amended to separate "modulate" into separate claims for identifying inhibitory drugs and enhancing drugs. New claims 74-79 are drawn to a subset of STAT proteins listed in claims 57-58 and 63-64. No new matter is added by this amendment, and reconsideration of the claims in view of the amendments and following remarks is respectfully requested.

### I. Response to Election/Restriction Requirement

Applicant's election with traverse of Group II was acknowledged. The requirement was made final, and claims 1, 60, and 61 were withdrawn as being drawn to a non-elected invention.

### II. Rejection Under 35 U.S.C. § 102(e)

**A.** Claims 56 and 59 were rejected as anticipated by McKnight et al. (US 5,710,266) on the basis that "McKnight et al. disclose an assay to determine drugs which modulate the dimerization of IL-4 STAT protein." Applicants respectfully traverse this rejection as it is applied to the amended claims 56 and 59, and to the new claims.

Under the standard required for anticipation under § 102, the cited prior art reference is required to disclose every element of the claimed invention. A reference that merely contains substantially the same elements is insufficient to "anticipate" the claimed invention. Jamesbury Corp. v. Litton Industrial Products, Inc., 225 USPQ 253 (Fed. Cir. 1985). Similarly, a reference that only broadly teaches the invention is also considered insufficient to establish anticipation. Kalman v. Kimberly-Clark Corp., 218 USPQ 781 (Fed. Cir. 1983). Further, an anticipatory reference must enable one skilled in the art to make the anticipated subject matter. PPG Industries, Inc. v. Guardian Industries Corp., 37 USPQ2d 1618 (Fed. Cir. 1996).

Claims 56 and 59. Amended claim 56 is drawn to a method for identifying a drug that enhances the ability of adjacent STAT protein dimers to interact comprising measuring the

ability of a test compound to enhance the association of a first STAT protein or a fragment of said first STAT protein with a second STAT protein or a fragment of said second STAT protein; wherein said fragment of said first STAT protein comprises the N-terminal domain of said first STAT protein;

wherein said fragment of said second STAT protein comprises the N-terminal domain of said second STAT protein; wherein the association is dependent upon the N-terminal domain of said first STAT protein, and the N-terminal domain of said second STAT protein; and wherein a test compound which enhances the association is identified as a drug that enhances the interaction between adjacent activated STAT dimers. New claim 66 similarly claims an inhibitory drug. Claim 59 and new claim 69 are drawn to the embodiment in which the first and second STAT proteins are the same.

McKnight et al. The cited McKnight et al. patent describes interleukin-4 peptides and methods for identifying agents which selectively bind the IL-4 peptide or receptor, including agents which disrupt IL-4 dimerization (col. 5). IL-4 corresponds to Stat6.

McKnight et al. do not disclose or suggest a method for identifying a drug that inhibits or enhances the ability of adjacent STAT protein dimers to interact.

Analysis. Applicants respectfully traverse this rejection on the basis that the instant claims describe a method which allows identification of a drug able to enhance or inhibit the interaction between adjacent activated STAT dimers. The instant claims describe a method for identifying a drug that modulates (e.g., enhances or inhibits) the ability of adjacent STAT protein dimers to interact, e.g., test for the formation of a higher order structure composed of two dimerized STAT protein complexes. McKnight et al. only refer to inhibition of dimer formation. See for example, col. 20, line 62 of McKnight et al., which states that no evidence of higher order (trimeric or tetrameric) oligomerization was observed. Accordingly, the McKnight reference cannot be held to anticipate the instant claims, and it is respectfully requested that this rejection be withdrawn.

**B.** Claims 56-59 were rejected as anticipated under 35 USC § 102(e) by Leonard (US 6,265,160). This rejection is respectfully traversed as it may be applied to the amended and

new claims.

The claims. Claims 56 and 59 are summarized above. Claims 57 and 58 (and new claims 67 and 68) each describe the first and second STAT proteins, respectively, as selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

Leonard US 6,265,160. Leonard describes the use of synthetic peptides which encompass the IL-2Rβ domains as able to inhibit Stat protein dimerization.

Leonard does not describe or suggest a method for identifying a drug that inhibits or enhances the ability of adjacent STAT protein dimers to interact.

Analysis. The above discussion is fully relevant to this rejection and is herein incorporated by reference. Leonard does not describe or suggest a method which allows identification of a drug able to enhance the interaction between adjacent activated STAT dimers. Nowhere in Leonard is there any anticipation of a higher order tetrameric structure. Indeed, the DNA binding assay described in Leonard is designed to demonstrate the presence of dimers (i.e., monomer-monomer complexes), not dimer-dimer complexes. Accordingly, the Leonard reference cannot be held to anticipate the instant claims, and it is respectfully requested that this rejection be withdrawn.

**Rejection Under 35 USC § 103(a)**

Claims 52-59 and 62-65 were rejected as obvious over Leonard in view of Xu et al. further in view of Schreiber et al. Applicants respectfully request clarification regarding the rejection of claims 52-59, since claims 52-55 were cancelled in the preliminary amendment filed 2 November 1999. This rejection is respectfully traversed as applied to pending claims 56-59 and 62-65 and new claims 66-79.

The invention as claimed. Claims 56-59 are summarized above. Claim 62 is drawn to a method for identifying a drug that enhances the ability of adjacent STAT protein dimers to interact comprising measuring the ability of a test compound to enhance the association of a fragment of a first STAT protein with a second STAT protein or a fragment of said second STAT protein dimer; wherein said fragment of said first STAT protein consists essentially of the

N-terminal domain of said first STAT protein; wherein said fragment of said second STAT protein comprises the N-terminal domain of said second STAT protein; wherein the association is dependent upon the N-terminal domain of said first STAT protein, and the N-terminal domain of said second STAT protein; and wherein a test compound which enhances the association is identified as a drug that enhances the interaction between adjacent activated STAT dimers. New claims 70 similarly describes a method for identifying an inhibitory drug.

Claims 63 and 64 (and new claims 71-72) identify the first and second STAT protein, respectively, as selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6. Claim 65 (and new claim 73) defines the first and second STAT protein as the same STAT protein.

The cited Leonard reference. The Leonard reference is summarized above.

Leonard does not describe or suggest a method for identifying a drug that inhibits or enhances the ability of adjacent STAT protein dimers to interact.

The cited Xu et al. reference. Xu et al. teaches that the amino terminal domain of STAT protein family members is required for dimerization and cooperative DNA binding.

The cited Schreiber et al. reference. Schreiber et al. describe a phosphorylated peptide able to bind and inhibit STAT-mediated transcription.

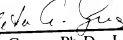
Analysis under § 103(a). Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness because none of the cited references, alone or in combination, provide an indication that the cooperative STAT binding leading to selectivity at certain promoters can be exploited for drug discovery. Leonard fails to disclose or suggest higher order associations between dimers, and indeed, could only identify the presence of monomer-monomer interactions. Xu et al. fail to cure the defects of Leonard because fail to provide any indication that the cooperative STAT binding leading to selectivity at certain promoters could be exploited for drug discovery. Schreiber et al. fail to cure the defects of Leonard and Xu et al. because the peptides described by Schreiber et al. act at the level of inhibition of dimer formation, not dimer-dimer interactions. Accordingly, in light of these remarks, it is believed that this rejection must be withdrawn.

**Conclusion**

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

In the event that there are any questions concerning this Amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,
KLAUBER & JACKSON



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56. (Amended Once) A method for identifying a drug that [modulates] enhances the ability of adjacent STAT protein dimers to interact comprising measuring the ability of a test compound to [modulate] enhance the association of a first STAT protein or a fragment of said first STAT protein with a second STAT protein or a fragment of said second STAT protein;

wherein said fragment of said first STAT protein comprises the N-terminal domain of said first STAT protein;

wherein said fragment of said second STAT protein comprises the N-terminal domain of said second STAT protein;

wherein the association is dependent upon the N-terminal domain of said first STAT protein, and the N-terminal domain of said second STAT protein; and

wherein a test compound which enhances the association is identified as a drug that enhances the interaction between adjacent activated STAT dimers[, whereas a test compound that decreases the association is identified as a drug that inhibits the interaction between adjacent activated STAT dimers].

57. The method of Claim 56 wherein said first STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

58. The method of Claim 56 wherein said second STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

59. The method of Claim 56 wherein said first STAT protein and said second STAT protein are the same STAT protein.

62. (Amended Once) A method for identifying a drug that [modulates] enhances the ability of adjacent STAT protein dimers to interact comprising measuring the ability of a test compound to [modulate] enhance the association of a fragment of a first STAT protein with a second STAT

protein or a fragment of said second STAT protein dimer;

wherein said fragment of said first STAT protein consists essentially of the N-terminal domain of said first STAT protein;

wherein said fragment of said second STAT protein comprises the N-terminal domain of said second STAT protein;

wherein the association is dependent upon the N-terminal domain of said first STAT protein, and the N-terminal domain of said second STAT protein; and

wherein a test compound which enhances the association is identified as a drug that enhances the interaction between adjacent activated STAT dimers[, whereas a test compound that decreases the association is identified as a drug that inhibits the interaction between adjacent activated STAT dimers].

63. The method of Claim 62 wherein said first STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

64. The method of Claim 62 wherein said second STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

65. The method of Claim 62 wherein said first STAT protein and said second STAT protein are the same STAT protein.

New claims:

66. (New) A method for identifying a drug that inhibits the ability of adjacent STAT protein dimers to interact comprising measuring the ability of a test compound to inhibit the association of a first STAT protein or a fragment of said first STAT protein with a second STAT protein or a fragment of said second STAT protein;

wherein said fragment of said first STAT protein comprises the N-terminal domain of said first STAT protein;

wherein said fragment of said second STAT protein comprises the N-terminal domain of said second STAT protein;

wherein the association is dependent upon the N-terminal domain of said first STAT protein, and the N-terminal domain of said second STAT protein; and

whereas a test compound that decreases the association is identified as a drug that inhibits the interaction between adjacent activated STAT dimers.

67. (New) The method of claim 66, wherein said first STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

68. (New) The method of claim 66 wherein said second STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

69. (New) The method of claim 66 wherein said first STAT protein and said second STAT protein are the same STAT protein.

70. (New) A method for identifying a drug that inhibits the ability of adjacent STAT protein dimers to interact comprising measuring the ability of a test compound to inhibit the association of a fragment of a first STAT protein with a second STAT protein or a fragment of said second STAT protein dimer;

wherein said fragment of said first STAT protein consists essentially of the N-terminal domain of said first STAT protein;

wherein said fragment of said second STAT protein comprises the N-terminal domain of said second STAT protein;

wherein the association is dependent upon the N-terminal domain of said first STAT protein, and the N-terminal domain of said second STAT protein; and

whereas a test compound that decreases the association is identified as a drug that inhibits the interaction between adjacent activated STAT dimers.

71. (New) The method of claim 70, wherein said first STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

72. (New) The method of claim 70, wherein said second STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 3, STAT 4, STAT 5A, STAT 5B, and STAT 6.

73. (New) The method of claim 71, wherein said first STAT protein and said second STAT protein are the same STAT protein.

74. (New) The method of claim 70, wherein said first STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 4, and STAT 6.

75. (New) The method of claim 70, wherein said second STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 4, and STAT 6.

76. (New) The method of claim 56 wherein said first STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 4, and STAT 6.

77. (New) The method of claim 56 wherein said second STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 4, and STAT 6.

78. (New) The method of claim 62 wherein said first STAT protein is selected from the group

consisting of STAT 1, STAT 2, STAT 4, and STAT 6.

79. (New) The method of claim 62 wherein said second STAT protein is selected from the group consisting of STAT 1, STAT 2, STAT 4, and STAT 6.